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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,974	OTSU ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-29* is/are pending in the application.

4a) Of the above claim(s) *21-23 and 26-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24 and 25* is/are rejected.

7)☒ Claim(s) *24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment of March 4, 2008, in response to the Action of October 4, 2007, is acknowledged. It is acknowledged that all prior claims have been cancelled and New Claims 21-29 have been added. Claims 21-23 and 26-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 24 and 25 are directed to the elected invention, a method for identifying an agent useful for treating cardiac failure, wherein the method analyzes ASK1 activity or autophosphorylation, and are herein examined.

Information Disclosure Statement

The US equivalent of JP10-000093, US 6,194,187, has been considered. If Applicants wish for JP10-000093 to be listed in the "References Cited" section of any patent that issues from this application, a supplemental Information Disclosure Statement should be filed.

Claims-Objections

For Claim 24, line 5, "collecting" would be better stated as "isolating".

For Claim 24, line 12, "used an indicator" should be corrected to "used as an indicator".

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

Claim 24 appears to be reciting several methods, using a variety of steps, for detecting ASK1 activity or auto-phosphorylation. The exact steps to be used in each method are unclear. For example line 5 recites "collecting...the ASK1 protein from cells", while line 7 recites "measuring kinase activity of the ASK1 protein in the cells". The ASK1 protein cannot both be collected from the cells and in the cells. The skilled artisan would not know the metes and bound of each recited method. The claims should be written such that each method of measuring ASK1 activity or auto-phosphorylation has clearly defined steps.

For Claim 24, line 5, "collecting or detecting...in the presence of a drug candidate compound is unclear". Is the ASK1 isolated or detected in the presence of the drug or are the cells treated with the drug prior to ASK1 isolation or detection? The skilled artisan would not know the metes and bound of each recited method.

Claim 24 is rendered indefinite by improper Markush language. In line 1, "prevention and treatment" should be corrected to "prevention or treatment".

For Claim 24, line 2-4, "selecting a medicinal component...from a drug candidate compound" is confusing because one cannot "select" from a group of one. Claim 25, as dependent from Claim 24, is indefinite for the same reason.

Claim 24 is rendered indefinite by referring to a sequence by a GenBank accession number. Sequences disclosed by accession numbers change over time; therefore, the skilled artisan would not be apprised of the metes and bounds of the recited invention. Claim 25, as dependent from Claim 24, is indefinite for the same reason. If the sequence Applicants mean to recite has been disclosed in the specification by a prior art publication that has been incorporated

by reference into the specification, Applicants may file a sequence listing disclosing said sequence and use the sequence identifier number (SEQ ID NO:) in the claims.

For Claim 24, penultimate line, the phrase "an amino acid sequence of GenBank…" renders the claim indefinite. It is unclear whether said phrase means "the amino acid sequence of GenBank…" or "any amino acid sequence of GenBank…", the latter being as small as a dipeptide. The skilled artisan would not be apprised of the metes and bounds of the recited invention. Claim 25, as dependent from Claim 24, is indefinite for the same reason. For purposes of examination, it is assumed that "an amino acid sequence of GenBank…" means "the amino acid sequence of GenBank…".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying agents that affect the kinase activity of AK1 using the method taught by Saitho et al, 1998, does not reasonably provide enablement for identifying agents that affect the kinase activity of AK1 using any method comprising any steps and reagents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 24 and 25 are so broad as to encompass identifying agents that affect the kinase activity of AK1, using any method comprising any steps and reagents. The scope of these claims is not commensurate with the enablement provided by the disclosure with regard to the very large number of methods, comprising an extremely large number of possible steps and reagents to be used. The specific reagents and steps used for detecting inhibition of any kinase activity determine the method's success. Predictability of which steps and reagents can be used to obtain the desired analysis requires a knowledge of, and guidance with regard to how said steps and reagents relate to the desired detection of kinase activity and inhibition thereof. However, in this case the disclosure teaches the steps and reagents of no such method; the art teaches the method of Saitho et al, 1998.

While some methods for identifying agents that affect the kinase activity of AK1 are known (Saitho et al), it is not routine in the art to screen numerous alterations in multiple steps and reagents for use in the methods encompassed by the instant claims. Furthermore, which steps and reagents can be altered with a reasonable expectation of success in obtaining the desired activity/utility are limited in any method and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to alteration in any steps or reagents of a method to diminish with each further alteration made.

The specification does not support the broad scope of Claims 24 and 25, which encompasses identifying agents that affect the kinase activity of AK1, using any method comprising any steps and reagents. The specification does not support the broad scope of Claims 24 and 25 because the specification does not establish: (A) any steps and reagents that can be used in a method to successfully identify agents that affect the kinase activity of AK1; (B) how

any steps and regents used in any successful method may or may not be altered and still obtain the desired analysis; (C) a rational and predictable scheme for developing or altering any method in order to obtain the desired analysis; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices of steps and regents are likely to be successful in identifying agents that affect the kinase activity of AK1.

Written Description

Claims 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 24 and 25 are directed to a genus of methods for identifying agents that affect the kinase activity of AK1, wherein the methods comprises any steps and reagents. The specification teaches the steps and reagents of no representative species of such methods. Moreover, the specification fails to describe any representative species of method by any identifying characteristics or properties other than the functionality of being a means for identifying agents that affect the kinase activity of AK1. Given this lack of description of representative species encompassed by the genera of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Saitoh et al, 1998. Saitoh et al teach methods for assaying ASK1 kinase activity and identifying inhibitors of

said activity, including thioredoxin (Fig 2; pg 2602, parg 4). Therefore, Claims 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Saitoh et al, 1998.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirotani et al, 2002 in view of Saitoh et al, 1998 as evidence by Sorescu et al, 2002. Hirotani et al teach that ASK1 mediates reactive oxygen species (ROS)-stimulated cardiac hypertropy. As evidence by Sorescu et al, said ROS-stimulated cardiac hypertrophy leads to left ventricular hypertrophy and heart failure (Abstract). Neither Hirotani et al nor Sorescu et al teach a method for assaying ASK1 activity. Saitoh et al teach methods for assaying ASK1 kinase activity and identifying inhibitors of said activity, including thioredoxin (Fig 2; pg 2602, parg 4). It would have been obvious to a person of ordinary skill in the art to use the methods of Saitoh et al to identifying inhibitors of ASK1 activity. Motivation to do so derives for the desire to screen for drugs useful in the prevention or treatment of cardiac failure. The expectation of success is high, as methods for assaying identifying inhibitors of the ASK1 taught by Saitoh et al were known in the art. Therefore, Claims 24 and 25 rejected under 35 U.S.C. 103(a) as being unpatentable over Hirotani et al, 2002 in view of Saitoh et al, 1998 as evidence by Sorescu et al, 2002.

In support of their request that said rejection, previously of Claim 7, be withdrawn, Applicants provide the following arguments.

(A) Hirotani et al teaches that (i) ASK1 has a broad range of biological activities, (ii) ASK1 activation leads to cell survival, and (iii) ASK1 is a stress-adaptation mediator in cardiomyoctes. Nothing in Hirotani et al suggests that ASK is involved in cardiac failure. The reference seems to suggest that the ASK1-mediated compensation mechanisms would teach away from identifying inhibitors of ASK1 in order to treat cardiac disease.

(B) Saitoh and Sorescu do not remedy the deficiencies of Hirontani. Sorescu in no way teaches that a drug inhibiting apoptosis induced by ASK1 would be useful in the treatment of cardiac disease. Sorescu teach that factors other than ASK1 stimulate hypertrophy.

(C) Applicants have unexpectedly found that inhibiting ASK1 is beneficial for prevention/treatment of cardiac failure.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: The fact that ASK1 has a broad range of biological activities in different cells does not detract from the teachings of Hirotani et al on the role of ASK1 in cardiac disease. Hirotani et al clearly teaches that ASK1 is involved in GPCR agonist-induced NF-kB activation and resulting hypertrophy in rat cardiomyocytes and that said result is mediated by ROS activating ASK1 (Abstract, last line; parg bridging pg 513-14).

(B) Reply: Sorescu et al is merely used in the rejection to show that, the fact that ROS-stimulated cardiac hypertrophy leads to left ventricular hypertrophy and heart failure, was known in the prior art (Abstract). Since, Hirotani et al teaches that ROS-stimulated NF-kB activation and cardiac hypertrophy is mediated by ASK1, (pg 510, parg 1; parg bridging pg 513-14), the skilled artisan would know that inhibitors of ASK1 would be useful for treating cardiac

disease. The fact that ASK1 has a broad range of biological activities in different cells does not detract from its role in cardiac disease.

(C) Reply: Applicants results are not unexpected; see (A), (B), and (D) herein and the prior action.

(D) Reply: It is noted that Applicants appear to believe that their invention is the discovery that ASK1 is a mediator of cardiac disease and, thus, a method for identifying inhibitors of ASK1 would have use in the development of treatment for cardiac disease. It is noted that the elected invention, methods for identifying inhibitors of ASK1, was known in the art (Saitoh et al, 1998). Applicants' development or "discovery" of the idea that inhibitors of ASK1 would have use in the treatment of cardiac disease is not patentable subject matter because said idea is none of a process, machine, manufacture, or composition of matter (MPEP 706.03(a)).

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
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